Cerebral arteriovenous malformations (AVMs) are uncommon vascular lesions in children, and differ pathologically from those occurring in adults. The exact prevalence and origin of pediatric cerebral AVMs remain unknown. While pediatric AVMs are presumed to occur during embryological development, only 18%–20% present before 15–20 years of age, with the majority remaining asymptomatic until 20–40 years of age, when they present with hemorrhage or seizures. The risk of hemorrhage in children has been reported to be 3.2% per year with 50%–80% of symptomatic AVMs in children presenting as hemorrhage. Resulting mortality from hemorrhage occurs at a rate of 20%–25% in children, which is higher than rates observed in adults, potentially due to varying locations of AVMs and more severe hemorrhage in children compared with adults. Treatment of AVMs includes complete elimination of the arterial nidus while attempting to preserve normal vasculature, and can be accomplished with resection or radiosurgery, either of which may be combined with endovascular embolization to make surgery more effective.
Intraoperative cerebral angiography in AVM resection in children

The goal of neurosurgery for AVMs is complete excision of the lesion while preserving adjacent brain parenchyma. Postoperative angiography was described by Allcock and Drake as early as 1963 to confirm successful surgical management of intracranial vascular lesions, because partially resected AVMs have an increased risk of hemorrhage in comparison with untreated AVMs. However, intraoperative angiography allows assessment of the surgical vascular bed, facilitating modification of surgical technique prior to cranial closure in cases of incomplete lesion resection, potentially eliminating the need for repeat craniotomy and surgery.

Intraoperative angiography was first described in 3 case reports by Loop and Foltz in 1966, and the first retrospective analysis performed by Grossart and Turner in 1973. Ghosh et al. published the first experience describing the use of intraoperative angiography in the pediatric population in 1998 and more recently, Ellis et al. demonstrated the safety and feasibility of the technique in children. Lastly, Lang et al. demonstrated the utility of intraoperative angiography in detecting residual AVMs in children by reporting equal recurrence rates for resected AVMs imaged using intraoperative angiography and those imaged with postoperative angiography. However, data on the safety and clinical utility of intraoperative angiography in the pediatric population remains limited in comparison with published data in adults.

Prior to the availability of intraoperative angiography at our institution, the imaging protocol included a diagnostic cerebral angiogram on the first postoperative day, followed by additional surgery if required. Currently, intraoperative angiography has replaced early postoperative angiography (within 24 hours) as the standard of care at our institution, with the first postoperative angiography now performed at 3 months following resection. This study is a single-institution retrospective consecutive cohort study describing the technique of intraoperative angiography in children, and evaluating diagnostic utility, procedure-related complications, and the effect of intraoperative angiography on surgical management.

Methods

Patient Population

Following approval by the institutional review board of the Children’s Hospital of Philadelphia, a retrospective review of the interventional radiology database was performed to identify all children who met the following inclusion criteria: diagnosis of cerebral AVM, which underwent resection; use of intraoperative angiography during AVM resection at our institution. The interventional radiology database includes all interventional procedures performed. A query of the database demonstrated the earliest intraoperative angiography to have been performed in January of 2008. Therefore all intraoperative angiographies performed between January 2008 and December of 2012 were included. Medical records were reviewed for all patients to confirm presence of a preoperative cerebral angiogram performed at our institution. Electronic medical and radiological records were reviewed for relevant clinical and procedural data.

Angiographic Technique

All procedures were performed on patients under general anesthesia in the operating room. Patients were placed supine and prepared and draped in standard fashion. Using ultrasound guidance, the common femoral artery was accessed using a 21-gauge single-wall needle. A 4.0-Fr or 5.0-Fr vascular sheath was placed, sutured in position, and secured with a sterile occlusive dressing during the neurosurgical procedure. A continuous low-dose heparin infusion (2 units/ml) was administered through the sheath at a rate of 2–4 ml/hour to maintain sheath and arterial patency. Patients then remained supine or were placed prone for the neurosurgical procedure, depending on the location of the neurovascular lesion. For patients placed in a prone intraoperative position, the short sheath was secured in a similar fashion. Following the neurosurgical procedure, the vascular sheath was accessed using a sterile technique, and a 4- or 5-Fr, Berenstein, JBI, or Harwood-Nash catheter (Cook Medical Inc.) was used for cerebral angiography depending on operator preference. Accessing the sheath in the prone position is challenging with a short sheath and our current practice modification is to use a long sheath (25 cm) and secure it to the side of the patient’s thigh. Single or two-vessel digital subtraction angiography was performed via hand injection using nonionic contrast media (Omnipaque 300, GE Healthcare) on a portable C-arm system with angiographic capability (Philips Medical Systems or GE Healthcare). Images were immediately interpreted by the radiologist and reviewed with the neurosurgeon.

Positive findings on intraoperative angiography following initial neurosurgical intervention included a residual arterial nidus, an early draining vein, or early visualization of the venous sinus, and allowed for modification of surgical technique. Repeat intraoperative angiography was performed following any additional neurosurgical intervention, and dural closure was completed following a negative intraoperative angiogram. The femoral sheath was removed using standard manual hemostatic techniques.

Resection was terminated when the surgeon believed the AVM nidus was completely resected and confirmation was achieved with intraoperative angiography. In lesions located in eloquent brain areas, the surgical approach was less aggressive and more dependent on the result of the intraoperative angiography.

Patient Follow-Up

Children were followed with postoperative angiography at 3-month, 1-year, and 5-year intervals following surgical management. For each patient, images from postoperative angiography were compared with those of intraoperative angiography to evaluate for accuracy of the intraoperative angiogram. Four patients had not yet received postoperative angiography at the completion of the study. For patients demonstrating an AVM on postoperative angiography, intraoperative images were reviewed to evaluate for residual disease to differentiate recurrent versus residual AVM on follow-up. Images were reviewed twice, first via 2-reader consensus, and then re-reviewed via 4-reader consensus to confirm the findings on intraoperative angiography.
Statistical Analysis

Comparison of dose-area product (DAP) and fluoroscopy times between intraoperative and postoperative angiography was performed using the Mann-Whitney U-test. Statistical significance was determined at $p \leq 0.05$.

Results

Patient Characteristics

Seventeen patients met eligibility criteria and were included in the analysis of intraoperative angiography. Patient demographics and clinical features are shown in Table 1.

Among the patients managed with intraoperative angiography, symptomatic hemorrhage was the most common presentation, and headache in the absence of hemorrhage was the second most common presentation. One patient presented with asymptomatic papilledema diagnosed during a routine eye examination, and 1 patient presented with increased head circumference and bulging fontanelles accompanied by vomiting and seizures from increased intracranial pressure. Three AVMs were recurrent from a previous resection and therefore presented asymptptomatically on routine follow-up imaging, while the fourth asymptomatic AVM was an incidental finding on imaging following head trauma. One child requiring a second resection of a recurrent AVM also required intraoperative angiography, and therefore underwent two intraoperative angiography sessions. All patients underwent pretreatment angiography, and their vascular anatomy is described in Table 1.

Treatment

Fourteen embolizations were performed preoperatively in 12 patients, with 2 patients receiving staged embolizations prior to surgery. In the 7 patients presenting with symptomatic hemorrhage, the median length of time from presentation to diagnostic angiography was 3 days (range 1–4 days), and the median length of time from presentation to surgical management was 3.9 months (range 5 days to 25.2 months).

Twenty-one successful intraoperative angiography procedures were performed in 17 children during 18 neurosurgical procedures. In 15 procedures, patients were supine, while in 3 they were prone. The technical success rate was 94%. One angiogram could not be completed due to a left vertebral artery dissection that occurred in 1 prone patient. Median fluoroscopy time for the 18 cases was 6.7 minutes (range 0.9–17.1 minutes), with 5 unknown values. Median DAP was 0.54 mGy-m$^2$ (range 0.2–1.8 mGy-m$^2$; Table 2), with 12 unknown values. Data for fluoroscopy time and DAP were not available for ear-

<table>
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</table>
Intraoperative cerebral angiography in AVM resection in children

Intraoperative angiography altered patient care in 2 (11%) of 18 neurosurgical procedures. Two repeat intraoperative angiograms were obtained during 1 AVM resection, and 3 repeat intraoperative angiograms were obtained in another. In the first procedure, 1 positive intraoperative angiogram demonstrating a large draining vein and persistent feeding vessels to the AVM resulted in 1 additional AVM resection (Fig. 1). In the second procedure, 2 positive intraoperative angiograms demonstrating early visualization of the internal cerebral vein resulted in 2 re-explorations and 1 surgical coagulation of a small abnormal-appearing nidal vein (Fig. 2). Hence, 21 intraoperative angiography sessions were performed during 18 neurosurgical procedures. Both patients in whom intraoperative angiography altered surgical management had no evidence of residual or recurrent neurovascular abnormality on the most recent follow-up angiography performed at 1 and 2.5 years, respectively.

The AVM demonstrated in Fig. 2 was a recurrent AVM. Therefore, although a small lesion, the decision was made to re-resect it using intraoperative angiography. The initial intraoperative angiogram demonstrated early opacification of the internal cerebral vein (Fig. 2B), and the first re-exploration intraoperatively did not demonstrate any nidal vessels. A second intraoperative angiography was performed to assess continued early visualization of the internal cerebral vein, which was still present, necessitating a second re-exploration. At that point a periventricular abnormal-appearing vein was isolated and surgically coagulated. The third intraoperative angiography session revealed no further early opacification of the internal cerebral vein. Follow-up at 2.5 years demonstrated no recurrent or residual disease.

A comparison of fluoroscopy time and DAP between single-vessel intraoperative angiography and conventional postoperative angiography performed in the same patient population is shown in Table 2. Dose-area products were available for 6 of 18 cases and fluoroscopy times were available for 13 of 18 cases. Six DAPs and 13 fluoroscopy times for postoperative angiography were chosen from the 17 patients in the cohort, accounting for both age and weight at the time of the procedure. A significant difference was observed between the DAP for intraoperative angiography in comparison with postoperative angiography (p = 0.004), while the fluoroscopy time was not statistically different between intraoperative and postoperative angiography. For conventional postoperative angiography, the protocol includes a complete angiogram of the bilateral anterior and posterior circulation. For intraoperative angiography, only the vessels of interest are imaged, accounting for the difference in DAP.

Complications

There was 1 major procedure-related complication for 21 intraoperative angiography sessions (4.8%), which was a left vertebral artery occlusion believed to be due to dissection in a prone patient with a dominant right vertebral artery. The nondominant left vertebral artery was inadvertently catheterized by the operator. Secondary thrombus formation extending into the basilar artery and bilateral posterior cerebral arteries was noted on CT angiography after the procedure. Follow-up imaging 5 days after intraoperative angiography revealed multiple infarcts in the posterior circulation and a small patent left vertebral artery.

Postoperative Follow-Up

To date 14 (78%) of 18 cases of neurosurgical management with intraoperative angiography have received follow-up postoperative angiography, with 3 of 4 patients not yet due for follow-up evaluation. Median follow-up time from intraoperative angiography to the first postoperative angiogram was 4 months (range 1 day to 8 months), and median follow-up time from intraoperative angiography to the most recent postoperative angiogram was 1.1 years (range 4.3 months to 3.8 years). Two (14%) of 14 postoperative angiograms were positive for the presence of an AVM at 3.5 and 4.7 months from intraoperative angiography. In the first case, postoperative angiography at 3.5 months postoperatively showed a faint arterial blush without associated early venous drainage suspicious for recurrent AVM, which was confirmed on 14-month follow-up imaging. In the second case, postoperative angiography at 4.7 months follow-up revealed a small AVM, which was found to enlarge on 1-year follow-up. Both patients underwent a second neurosurgery for AVM resection and postoperative angiography at 1-year follow-up showed no residual or recurrent anomalies. For both patients with positive postoperative angiograms on follow-up, the intraoperative angiogram was reviewed via 2-reader consensus followed by 4-reader consensus and confirmed to be negative, without disagreement, indicating probable recurrent rather than residual disease.

Discussion

The importance of postoperative imaging to confirm

<table>
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<th>TABLE 2: Comparison of DAP and fluoroscopy times between intraoperative and postoperative angiography*</th>
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<tr>
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<td>fluoroscopy time (min) (n = 13)</td>
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* NS = nonsignificant.
complete neurosurgical resection has been documented by several authors, with Allcock and Drake being the first to describe such an idea in 1963 for the treatment of cerebral aneurysms. The benefits of intraoperative angiography include the ability to assess for and address a residual vascular lesion prior to dural closure, thereby reducing the risk of complications from residual lesions, and potentially eliminating the need for future surgeries and associated surgical complications.

However, the use of routine intraoperative angiography remains controversial, and has been described in a limited fashion in the pediatric population. Although some authors have recommended selective use of intraoperative angiography, 4.4% of adult patients not chosen to receive intraoperative angiography following aneurysm repair had residual disease requiring intervention, as described by Klopfenstein et al.

The current study demonstrated a surgical correction rate of 11%, with 2 of 18 cases meriting altered surgical management as a result of findings on intraoperative angiography. A review of the literature has demonstrated correction rates of 19% (4/22 cases), 22.2% (4/18), and 22.7% (5/22 cases) in 3 previously published studies evaluating intraoperative angiography in children. Intraoperative angiography changed management in 10.4%—29% of AVM resections in the adult population.

Additional studies in the adult population assessed the use of intraoperative angiography in a wider distribution of cerebrovascular anomalies including arteriovenous fistulas and in patients requiring carotid endarterectomies. Barrow et al. described 115 cases of neurovascular anomalies, 19 of which required further surgical management, and 14 of which consisted of AVMs and aneurysms. Derdeyn et al. described 112 total neurovascular procedures in which intraoperative angiography changed management in 5 of 18 AVMs, 5 of 66 aneurysms, and 3 of 28 endarterectomies. Yanaka et al. reported altered...
management after intraoperative angiography in 1 (5%) of 20 cases of AVMs and arteriovenous fistulas.39

Intraoperative angiography is not without complications, which include stroke, arterial dissection, emboli, and hematoma.23 Complication rates described in earlier pediatric studies were 4.5%44 and 3.3%,29 and those reported in the adult population ranged from 0.4% to 3.7%.1,7,9,22,23,25,32,36,37

The complication rate of 4.8% in our study was slightly higher than total complication rates previously reported. However, this may be attributable to the small sample size of the current study.

Although intraoperative angiography may play an important role in resection of cerebrovascular anomalies, the literature emphasizes inferior image quality in intraoperative angiography in comparison with that of postoperative angiography.21 Limiting factors include suboptimal fluoroscopic visibility, contrast via hand injection, nonstandard patient positioning, and artifacts from surgical equipment.21,39 Even with advances in available technology and improved imaging equipment increasing the reliability of intraoperative angiography,39 postoperative angiography has been considered the gold standard in the management of neurovascular anomalies.21 Ellis et al. described a false negative rate of 6.25% for intraoperative angiography in the pediatric population, with 1 of 15 patients demonstrating a positive postoperative angiogram.12 In the management of adult AVMs and aneurysms, the literature describes a false negative rate for intraoperative angiography of 4.8%–5.2%.28,37

However, Lang et al. compared results of postoperative angiography in children who received intraoperative angiography during AVM resection and those who received postoperative angiography on the first day following resection. This study reported similar rates of positive postoperative angiography in both groups, demonstrating intraoperative angiography to be equally sensitive to postoperative angiography for confirming complete AVM resection.26

Several large studies have concluded that patients with complete AVM resection confirmed by negative postoperative angiography do not develop recurrent bleeds.8,11,16,19,38 However, there have been a small number of reported cases of recurrent AVMs following presumed complete resection confirmed by postoperative angiography in the pediatric population.5,20,24 In the current study, the rate of negative intraoperative angiography found to be positive on follow-up postoperative angiography was 14%, indicating probable recurrence in these patients.

Recurrences in the pediatric population are reported to occur early.20 The majority of children with negative postoperative angiography at 3 and 6 month follow-up imaging were not found to have recurrent AVMs on further follow-up as reported by Lang et al. However, positive postoperative angiography at approximately 1-year follow-up did occur in a small number of children with negative postoperative angiography at 3 and 6 months postoperatively, emphasizing the importance of postoperative angiography at 1 year in children.26 Furthermore, Lang et al. reports a strong correlation between a low compactness score and the risk for recurrence following complete AVM resection, with diffuse AVMs being more likely to recur.26

Ali et al. reviewed several large pediatric studies and reported a mean of 5.5 years from initial AVM resection to a secondary recurrence in children,2 with a range of 1–9 years.29 However, follow-up was performed using MRI, which is not as sensitive for detection of AVMs as cerebral angiography.

The mechanism underlying recurrent AVMs remains unknown. Whether recurrent lesions occur as a de novo malformation or from a residual, angiographically invisible nidus remains unclear.4 The literature describes several factors as potentially contributing to recurrent AVMs, including the immaturity of the growing pediatric cerebrovascular system.30 Hino et al. suggest that small immature vessels, retaining the capability to grow and form another AVM, may have been left in the surgical field.17 Alternative ideas include stimulation of angiogenesis by brain injury, tumors, or inflammation,13,33 as well as by inappropriate expression of humoral growth factors such as vascular endothelial growth factor.5,23,34,35

Conclusions

Intraoperative angiography is an effective and safe adjunct for surgical management of cerebral AVMs in children. Demanding conditions of the intraoperative angiography technique in comparison with postoperative angiography require angiographers with experience and diagnostic acumen; however, the results obtained appear to improve surgical management of neurovascular anomalies in children and reduce both the risks associated with incomplete resection of cerebrovascular anomalies and the need for additional surgery.

Disclosure

Dr. Ichord is a member of the Clinical Event Committee for the Berlin EXCOR pediatric IDE trial.

Author contributions to the study and manuscript preparation include the following. Conception and design: Cahill. Acquisition of data: Gaballah, Rabinowitz, Cahill. Analysis and interpretation of data: Gaballah, Storm, Rabinowitz, Ichord, Cahill. Drafting the article: Gaballah, Storm, Ichord, Cahill. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Gaballah. Study supervision: Cahill.

References